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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,281	10/30/2003	Paul K. Wolber	10030355-1	3574

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EXAMINER	
CROW, ROBERT THOMAS	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/699,281	WOLBER ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *14-20 and 26-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/30/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in papers filed 26 January 2006 is acknowledged. Applicant argues that it would not be undue burden to examine the claims of Groups I and III along with claims of Group I as evidenced by the fact that the claims of Groups I-III have acquired a separate status in the art as recognized by their different classifications, as recognized by their divergent subject matter, and/or because a search of the subject matter of Group I is not co-extensive with a search of Groups II and III. For example, a search for Group I would involve searching quality evaluation, depurination probe features, and determination of relative amounts. In contrast, Group II requires searching for tethers, oligonucleotide lengths, and tether domains. Finally, Group III requires searching the computer art for readable media, programming, and signal detection. The searches for Groups I-III are clearly not coextensive and thereby impose a serious collective burden on the examiner.

The requirement is still deemed proper and is therefore made **FINAL**.

Claims 14-20, and 26-28 are therefore withdrawn. Claims 1-13 and 21-25 are currently under prosecution.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claims 1-13 are indefinite in independent claim 1, which recites the limitation "the amount" in line 7 of claim 1. There is insufficient antecedent basis for this limitation in the claim. It is suggested that the word "the" be changed to "an."

2. Claim 3 is indefinite in the recitation "a relative amount" at the end of the claim. It is unclear what quantity the amount is relative to.

3. Claim 8 is indefinite in the recitations "early" and "late" in line 2 of the claim. It is unclear how "early" and "late" modify the depurination probe features; e.g., if 'early" relates to position on the array, position within a sequence, chronological time of synthesis, etc.

4. Claims 21-25 are indefinite in claim 21, which recites the limitation "the surface" in line 7 of claim 21. It is suggested that the word "the" be changed to "a." Claims 21-25 are also indefinite in claim 21, which recites the limitation "said analyte" in the last line

of the claim. It is suggested that the term "said analyte" be changed to "said nucleic acid analyte."

5. Claim 22 is indefinite in the recitation "said depurination probes nucleic acids" in lines 2-3 of the claim. There is insufficient antecedent basis for this limitation in the claim. It is suggested that the word "said" be removed from the claim. Claim 22 is also indefinite because it is unclear if the sample further comprises the target nucleic acid in addition to the analyte of claim 22.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1-7, 11-13 and 21-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Church et al (U.S. Patent No. 6,326,489 B1, issued 4 December 2001).

Regarding claim 1, Church et al teach the method of detecting the presence of depurination reaction products on a surface of an in situ produced nucleic acid array, said method comprising: contacting an in situ produced nucleic acid array (e.g., a photolithographically produced nucleic acid array; column 7, lines 1-33) that includes at

least one depurination probe feature of a depurination probe (e.g., an oligonucleotide containing a sequence comprising an adenine is removed from the array; Figure 4) with a sample comprising a target nucleic acid that specifically binds to said depurination probe (e.g., an oligonucleotide is hybridized to said array; column 3, lines 56-59); and detecting the amount of resultant binding complexes in said depurination probe feature to determine the presence of depurination products on said surface (e.g., the double-stranded hybridization complex is cleaved with RsaI, thereby releasing an adenine from the array [i.e., resulting in depurination], and the amount of cleavage is detected by loss of a fluorescence signal; column 13, line 63-column 14, line 12).

Regarding claim 2, Church et al teach the method of claim 1, wherein said method is a method of determining the amount of depurination the amount of depurination reaction products on said surface (e.g., the method allows detection of cleavage of the surface strands; column 13, line 63-column 14, line 12 and Figure 4).

Regarding claim 3, Church et al teach the method of claim 2, wherein said amount is a relative amount (e.g., the amount of cleavage I detected via loss of a fluorescent signal, wherein a dark area on the chip indicates cleavage relative to the earlier scan of the chip, which exhibited fluorescence prior to cleavage; column 13, line 50-column 14, line 12 and Figures 3 and 4).

Regarding claim 4, Church et al teach the method of claim 1, wherein said target nucleic acid is labeled (e.g., the second strand is labeled, column 13, lines 33-40) and said detecting comprising detecting a signal from said depurination probe feature (e.g.,

fluorescence is detected before and after cleavage with RsaI; column 13, line 63-column 14, line 12 Figure 4).

Regarding claim 5, Church et al teach the method of claim 4, wherein said label is fluorescent (e.g., fluorescein; column 13, line 38) and said signal is a fluorescent signal (e.g., fluorescence is detected; column 14, lines 5-10).

Regarding claim 6, Church et al teach the method of claim 5, wherein said fluorescent signal has an intensity that is inversely proportional to the amount of depurination reaction products in said depurination probe feature (e.g., when depurination [i.e., cleavage with RsaI] has occurred, scanning of the array results in a dark area, so that zero fluorescence positively indicates cleavage and detectable fluorescence indicates no cleavage; column 13, lines 50-column 14, line 10).

Regarding claim 7, Church et al teach the method of claim 1, wherein said array includes two or more different depurination probe features each corresponding to a distinct depurination probe (e.g., the array has a plurality of nucleic acids; Abstract, lines 1-4).

Regarding claim 11, Church et al teach the method of claim 1, wherein said method further comprises evaluating the level of depurination that occurred during in situ fabrication of said array (e.g., in situ fabrication of the array is complete after the RsaI cleavage step, which detects the amount of depurination [i.e., RsaI cleavage]; column 13, lines 50-column 14, line 10).

Regarding claim 12, Church et al teach the method of claim 11, wherein said method is a method of evaluating the quality of an in situ nucleic acid synthesis fabrication protocol (e.g., RsaI cleavage is used to detect synthesis of the second strand; column 13, lines 50-column 14, line 10).

Regarding claim 13, Church et al teach the method of claim 12, wherein said method is employed to evaluate the quality of a plurality of nucleic acid arrays fabricated according to said protocol (e.g., the method is used as evidence of successful second strand synthesis for arrays of the invention [emphasis added by the Examiner]; column 14, lines 18-23)

Regarding claim 21, Church et al teach the method of detecting the presence of a nucleic acid analyte in a sample, said method comprising: contacting a nucleic acid array comprising a set of two more nucleic acid depurination features (e.g., a photolithographically produced nucleic acid array [column 7, lines 1-33] comprising a plurality of nucleic acids [Abstract, lines 1-4]) having a nucleic acid ligand that specifically binds to said nucleic acid analyte (e.g., the array has a plurality of immobilized nucleic acids [Abstract, lines 1-4] that hybridize to primers [column 3, lines 18-21]) with a sample suspecte3d of comprising said analyte under conditions sufficient for binding of said analyte to said nucleic acid ligand on said array to occur (e.g., primers are hybridized to the array; column 3, lines 18-21); and detecting the presence of binding complexes on the surface of said array to detecting the presence of said analyte in said sample (e.g., the primers are used to synthesize a second strand [column

3, lines 55-63]; and the second strand is detected using RsaI cleavage [column 13, line 63-column 14, line 12]).

Regarding claim 22, Church et al teach the method of claim 21, wherein said sample comprises a collection of labeled target nucleic acids that specifically bind to said depurination proves nucleic acids (the primers bind to the array, extended, and labeled; column 13, lines 33-50).

Regarding claim 23, Church et al teach the method of claim 21, wherein a result from reading of an array is transmitted from a first location (e.g., the surface of the array) to a second location (e.g., an argon laser confocal scanner; column 13, lines 50-55).

Regarding claim 24, Church et al teach the method of claim 23, wherein said second location is a remote location (e.g., an argon laser confocal scanner; column 13, lines 50-55).

Regarding claim 25, Church et al teach the method of claim 21, wherein a transmitted result of reading an array is received (e.g., an argon laser confocal scanner scans the array and the data is transmitted so that it can be photographed; column 13, lines 50-55 and Figure 4).

2. Claims 21 is rejected under 35 U.S.C. 102(b) as being anticipated by McGall (U.S. Patent No. 5,843,655, issued 1 December 1998).

Regarding claim 21, McGall teaches the method of detecting the presence of a nucleic acid analyte in a sample, said method comprising: contacting a nucleic acid

array, said array comprising a set of two or more nucleic acid depurination features (e.g., a nucleic acid array produced photolithographically [Figure 1] that includes at least one depurination probe feature of a depurination probe [e.g., depurinated oligonucleotides; Abstract, lines 4-5]) having a nucleic acid ligand that binds specifically to said nucleic acid analyte under conditions sufficient for binding of said analyte to said nucleic acid ligand on said array to occur (e.g., samples are exposed to arrays under hybridization conditions; column 1, lines 30-37); and detecting the presence of binding complexes on the surface of said array to detect the presence of said analyte in said sample (column 1, lines 35-36).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not

commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. Claims 1-13 and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over McGall (U.S. Patent No. 5,843,655, issued 1 December 1998) in view of Church et al (U.S. Patent No 6,326,489 B1, issued 4 December 2001).

Regarding claim 1, McGall teaches a method of detecting the presence of depurination reaction products on a surface of an in situ produced nucleic acid array, aid method comprising: contacting an in situ produces nucleic acid array (e.g., a nucleic acid array produced photolithographically; Figure 1) that includes at least one depurination probe feature of a depurination probe (e.g., depurinated oligonucleotides; Abstract, lines 4-5) with a sample that allows detection of the presence of depurination products on said surface (e.g., the array is exposed to a test condition that allows determination of the extent of depurination; column 2, lines 48-62). McGall also teaches that the arrays are used for hybridization (column 1, lines 30-44). While McGall also teaches that test conditions comprise operating conditions (column 11, lines 35-41) and that operating conditions of the array includes hybridization of nucleic acids to the array (column 1, lines 30-44), McGall does not explicitly show hybridization as a test condition.

However, Church et al teach oligonucleotide arrays (e.g., a photolithographically produced nucleic acid array; column 7, lines 1-33) that operate by hybridization (e.g., an oligonucleotide is hybridized to said array; column 3, lines 56-59) and allow detection of hybridization (column 13, line 63-column 14, line 12) with the added benefit that the hybridization conditions allow the array to be used for detecting DNA binding proteins of clinical interest (column 14, lines 47-56).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the depurination detection test conditions as taught by McGall under hybridization conditions as taught by Church et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in testing conditions that allow the array to be used for detecting DNA binding proteins of clinical interest as explicitly taught by Church et al (column 14, lines 47-56).

Regarding claim 2, the method of claim 1 is discussed above. Mc Gall also teaches that the method detects the amount of depurination products on said surface (column 2, lines 48-50).

Regarding claim 3, the method of claim 2 is discussed above. McGall also teaches the detection of a relative amount (column 7, lines 63-67).

Regarding claim 4, the method of claim 2 is discussed above. McGall also teaches the labeling of the target nucleic acid (column 11, lines 55-56).

Regarding claim 5, the method of claim 4 is discussed above. McGall also teaches fluorescent labels and signals (column 3, lines 24-31).

Regarding claim 6, the method of claim 5 is discussed above. McGall also teaches a fluorescent signal having an intensity inversely proportional to the amount of depurination products present (column 9, lines 65-67).

Regarding claim 7, the method of claim 1 is discussed above. McGall also teaches an array including two or more different depurination probe features each corresponding to a distinct depurination probe (e.g., the array has a plurality of nucleic acids; column 1, lines 30-44).

Regarding claim 8, the method of claim 1 is discussed above. McGall also teaches early and late depurination probe features (e.g., the depurination features occur at positions in the sequence relative to the surface; Figures 8 and 9).

Regarding claim 9, the method of claim 1 is discussed above. McGall also teaches arrays including two or more features whose synthesis was started at different times (areas on the surface are sequentially synthesized; column 9, lines 30-35).

Regarding claim 10, the method of claim 1 is discussed above. McGall also teaches a known deblock dose (e.g., selective deprotection and coupling cycles are repeated until the desired products are obtained [column 5, lines 2-25], the desired products requiring a known number of cycles).

Regarding claim 11, the method of claim 1 is discussed above. McGall also teaches the method further comprises evaluating the level of depurination that occurred during in situ fabrication of said array (column 2, lines 48-50).

Regarding claim 12, the method of claim 11 is discussed above. McGall also teaches the method is a method of evaluating the quality of an in situ nucleic acid array synthesis protocol (column 1, lines 7-9).

Regarding claim 13, the method of claim 12 is discussed above. McGall also teaches the method is employed to evaluate the quality of a plurality of nucleic acid arrays fabricated according to said protocol (e.g., arrays in different test areas on the substrate are independently evaluated; column 9, lines 38-49).

Regarding claim 22, McGall teaches the method of detecting the presence of a nucleic acid analyte in a sample, said method comprising: contacting a nucleic acid array, said array comprising a set of two or more nucleic acid depurination features (e.g., a nucleic acid array produced photolithographically [Figure 1] that includes at least one depurination probe feature of a depurination probe [e.g., depurinated oligonucleotides; Abstract, lines 4-5]) having a nucleic acid ligand that binds specifically to said nucleic acid analyte under conditions sufficient for binding of said analyte to said nucleic acid ligand on said array to occur (e.g., samples are exposed to arrays under hybridization conditions; column 1, lines 30-37); and detecting the presence of binding complexes on the surface of said array to detect the presence of said analyte in said sample (column 1, lines 35-36); i.e., McGall teaches the method of claim 21. In

addition, McGall teaches labeled target nucleic acids (column 11, lines 55-56). McGall also teaches that test conditions comprise operating conditions (column 11, lines 35-41) and that operating conditions of the array includes hybridization of nucleic acids to the array (column 1, lines 30-44), McGall does not explicitly show hybridization as a test condition.

However, Church et al teach oligonucleotide arrays (e.g., a photolithographically produced nucleic acid array; column 7, lines 1-33) that operate by hybridization (e.g., an oligonucleotide is hybridized to said array; column 3, lines 56-59) and allow detection of hybridization (column 13, line 63-column 14, line 12) with the added benefit that the hybridization conditions allow the array to be used for detecting DNA binding proteins of clinical interest (column 14, lines 47-56).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the depurination detection test conditions as taught by McGall under hybridization conditions as taught by Church et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in testing conditions that allow the array to be used for detecting DNA binding proteins of clinical interest as explicitly taught by Church et al (column 14, lines 47-56).

Regarding claim 23, the method of claim 21 is discussed above. McGall also teaches transmitting a result from a reading of an array according to the method of

claim 21 from a first location (e.g., the surface of the array) to a second location (e.g., a line scanner; column 12, lines 56-67).

Regarding claim 24, the method of claim 23 is discussed above. McGall also teaches the second location is a remote location (e.g., a line scanner; column 12, lines 56-67).

Regarding claim 25, the method of claim 21 is discussed above. McGall also teaches receiving a transmitted result (e.g., images are stored in a computer; column 12, lines 56-67).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571) 272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert T. Crow
Examiner
Art Unit 1634

BJ FORMAN, PH.D.
PRIMARY EXAMINER